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Effects of gender-related factors on the incidence of localized alveolar osteitis

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Numerous literature references have suggested increased risk for localized alveolar osteitis associated with female gender, use of oral contraceptives, and point in menstrual/contraceptive cycle. However, the available information has not been systematically considered with the intent to accurately estimate the magnitude of these effects. The present review suggests that under certain conditions, some of which may be avoidable, females may have at least a two to threefold increase in osteitis risk compared with males. It appears that this greater risk may be reduced by considering hormonal cycles when scheduling elective exodontia. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;79:416-22)**

Localized alveolar osteitis (AO, dry socket) is a complication observed most often after mandibular third molar extractions. It is a condition of severe pain at the extraction site that usually begins 2 to 3 days after surgery, many times in the presence of a necrotic odor and a grayish discharge.[1] The cause is related to fibrinolysis of the clot possibly associated with bacterial invasion.[2] The pain is frequently refractory to routine postextraction analgesics and, for at least 45% of AO patients, four or more appointments (for irrigation and placement of sedative dressings) are required for complete resolution of symptoms.[3]

Considerable efforts have been made to estimate the incidence of AO and to determine relevant risk factors. Surgical difficulty, experience of the surgeon, tooth location, tobacco use, female gender, oral contraceptives (OC), point in menstrual cycle, corticosteroid use, local anesthetics with a vasoconstrictor, presurgical pathologic factors, and the omission of various prophylactic measures have all been cited as contributing to the occurrence of AO.[2, 4-8]

Despite numerous studies in which gender-related effects have been evaluated, conclusions are equivocal. Factors contributing to interpretive difficulty are: lack of consistency in diagnostic and surgical expertise across studies, unreliability and lack of statistical power as a result of small sample sizes, unknown OC use, limited information concerning the temporal relationship between day of surgery and OC/menstrual cycle, and lack of control for known confounders.

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It is the intent of this review to consider all relevant experimental studies in order to provide reliable estimates of gender-related effects on AO rates. However, estimates based on a combination of historic reports are subject to a wide variety of complications. Since Krough's[9] 1937 report, there have been dramatic changes in surgical and antimicrobial methods. Furthermore, the numerous studies differ with respect to sites and nature of extractions, clinical method and characteristics studied, the explicitness of the data reported, and the nesting of extraction sites within patients, which has implications for the design of valid statistical methods. In many studies, gender was essentially a nuisance factor the effects of which were reported as merely an ancillary finding relative to the manipulations of primary interest.

Because of these methodologic differences, one would not expect consistency in incidence rates. However, primary attention is directed here to differences in rates across gender and, for that reason, primary interest will be directed to odds ratios (ORs) where males (M) define the referent group and females (F, unspecified with respect to OC), females not using OC (FC−), and females using OC (FC+) are the comparison groups.

With respect to OC, it would appear that female subjects have been categorized as to use versus nonuse, but information pertaining to content and dosage was not typically sought. However, between 1964 and 1984, 42 brands of OC were marketed in the United States that differed in both content (one of nine types of progestin and one of two types of estrogen or no estrogen at all) and dosage. Furthermore, prescribed dosages have generally decreased in strength and potency over time.[10] These changes, as well as the recent availability of injectable and implantable contraceptives, suggest that when one studies the effects of

Table I. Incidence of alveolar osteitis by sex, oral contraceptive use, and menstrual cycle

Author	Design type*	Male		Female: OC not used		Female: OC used		Female: Unspecified	
		AO (%)	AO/Total	AO (%)	AO/Total	AO (%)	AO/Total	AO (%)	AO/Total
Krough[9]	abC	2.05	57/2785†	2.24	81/3618†				
MacGregor[4]	aBC	4.22	115/2723					6.50	86/1324
Schow[14]	ABC	15.38	96/624	20.49	59/288	44.64	75/168		
Lilly et al.[15]	Abc	8.19	124/1514	7.16	35/489	21.35	41/192		
Butler and Sweet[16] (175 ml lavage)	ABc	5.66	6/106	4.60	4/87	11.11	2/18		
Butler and Sweet[16] (25 ml lavage)	ABc	11.32	12/106	6.90	6/87	27.78	5/18		
Sweet and Butler[18] (all data)	Abc	0.54	1/186	3.42	8/234	5.95	5/84		
Sweet and Butler[18] (175 ml lavage)	ABc	1.08	1/93					3.14	5/159
Sweet and Butler[18] (350 ml lavage)	ABc	0.00	0/93					5.03	8/159
Gersel-Pedersen[19]	Abc	3.08	4/130	12.77	12/94	31.25	5/16		
Catellani et al.[20] (Day 1-22)	AbCd					31.03	18/58		
Catellani et al.[20] (Day 23-28)	AbCd					0.00	0/13		
Nordenram and Grave[21] (Day-1)	ABCD			17.95	7/39	28.21	11/39		
Nordenram and Grave[21] (Day-14)	ABCD			7.69	3/39	17.95	7/39		
Brekke et al.[22] (PLA−)	ABc	11.24	10/89					19.42	27/139
Brekke et al.[22] (PLA+)	ABc	2.25	2/89					4.32	6/139
Field et al.[23]	abC	3.40	45/1322					5.55	40/721
Fridrich and Olson[24]	Abc	15.97	76/476†	11.30	40/354†	21.31	26/122†		
Herpy and Goupil[25]	AbC	14.00	21/150					19.82	22/111
Al-Khateeb et al.[7]	abC	18.14	80/441†	16.85	31/184†	23.53	4/17		
Larsen[26]	Abc	10.66	13/122	20.37	22/108	10.42	5/48		
Larsen[2]	AbC	14.00	7/50	25.00	9/36	18.75	3/16		

*a = Assorted site types, A = Mandibular molars only; B = multiple sites/patient, B = One site/patient; c = Clinical trial of dry socket preventative, C = Observational study of dry socket incidence; d = point in menstrual cycle a between-subjects variable, D = Point in menstrual cycle a within-subjects variable.
†Counts were estimated from reported percentages (see text).

"steroidal" contraceptives one is studying a moving target.

If multiple extraction sites are nested within subjects, potential intraclass correlations ordinarily preclude valid estimates of P-values and confidence intervals (CIs) associated with estimates of ORs. Though methods have been recently developed for correct inferential analysis,[11-13] the studies reviewed here do not usually provide sufficient data detail for their implementation. However, when only one site per patient has been studied or when such data can be constructed by stratifying results (for example, data are segregated into two treatments randomly assigned to bilateral third molars), these data are reported. Methods and data from 16 studies are described below and in Table I.

CHRONOLOGICALLY ORDERED HISTORIC FINDINGS

The first study of AO incidence rate was undertaken in 1937 by Krough[9] who evaluated 6403 routine dental extractions (most were not third molars) in 2110 patients. These extractions were distributed among 917 males and 1193 females. Of 138 dry sockets, 57 (41.3%) were in males and 81 (58.7%) were in females. OC were nonexistent when these data were collected (1929 to 1936). Krough concluded that males and females have the same susceptibility to AO because these proportions were similar to patient size proportions (917/2110 = 43.5% of patients were males and 1193/2110 = 56.5% were females), apparently assuming that the average number of extractions per patient were the same in both gender groups. On the basis of this assumption, there were 57 cases of AO among 0.435(6403) = 2785 extractions in males (2.05%) and 81 cases among 0.565(6403) = 3618 extractions in females (2.24%).

In 1968 MacGregor[4] also undertook a large and complex study of AO at multiple assorted sites within patients. However, data are provided for an easily analyzable subset of his findings that only considered 4047 patients with single extractions. There were 2723 males, of whom 115 had AO (4.22%) and 1324 females, 86 of whom had dry sockets (6.50%). The observed sex effect may have been due to some females using OC, but this information was not collected.

In 1974 Schow[14] restricted his study of AO to mandibular third molars; he also stratified females according to OC usage. For M, FC−, and FC+ sub-

jects, AO rates were 15.38% (96/624), 20.49% (59/288), and 44.64% (75/168), respectively. Schow reported 1080 procedures but did not report the number of patients directly. However, he noted that, "Two hundred and thirty patients (21.9%) had pain . . . ." Because he used "patients" here rather than "teeth," it would appear that the 1080 sites were observed in 230/0.219 = 1050 patients. Thus for practical purposes one site per patient was being studied.

In 1974 Lilly et al.[15] restricted attention to 2195 mandibular third molars extracted from 1358 patients. In addition to stratifying on a variety of clinical features, they also studied the effects of oral lavage and OC use. Collapsing across all these variables, the AO rates for M, FC−, and FC+ were 8.19% (124/1514), 7.16% (35/489), and 21.35% (41/192), respectively.

In 1977 Butler and Sweet[16] (it appears that the same female data were reported by Sweet and Butler[17]) studied 106 males and 105 females where, in each case, one of two extracted bilateral mandibular molar sites received a 25 ml lavage whereas the other received a 175 ml lavage. Collapsing across the significant lavage effect, AO rates were 8.49% (18/212), 5.75% (10/174), and 19.44% (7/36), for M, FC−, and FC+, respectively. Table I reports findings by each lavage subgroup because data stratified in this way only consider one site per patient.

In 1978 Sweet and Butler,[18] in studying the effects of two different volumes of an antimicrobial mouth rinse (as a within subject variable) on AO rates, observed 504 mandibular third molar extractions in 93 males and 159 females (all bilateral extractions). Again, collapsing across the main experimental variable, AO rates were 0.54% (1/186), 3.42% (8/234), and 5.95% (5/84) for M, FC−, and FC+, respectively. Sweet and Butler did not tabulate lavage outcomes by the gender/oral contraceptive groups but did do so by gender alone. These one site per patient data are shown in Table I.

Gersel-Pedersen[19] studied the therapeutic effect of trans-4-amino-methyl cyclohexane acid in the extraction of 120 bilateral mandibular third molars in a within-subjects design. Osteitis was divided into two categories: alveolitis sicca dolorosa (ASD) and exudative alveolitis (EA). In the 240 sites there were 15 cases of ASD and 21 cases of EA. For purposes of this article these events would ordinarily be combined. However, the author reported no sex-related differences in ASD rate and apparently for that reason did not report counts by gender. It was parenthetically reported, though, that no cases of ASD occurred among 13 women treated during their menstrual period. For EA there was an observed sex effect with rates for M, FC−, and FC+ being 3.08% (4/130), 12.77% (12/94), and 31.25% (5/16), respectively. Sufficient information to reconstruct one site per patient data on a gender basis were not available within this study.

Catellani et al.[20] conducted an observational study of 71 third molar extractions in 47 women taking OC. AO rates for days 1 to 22 when oral contraceptive tablets were taken versus days 23 to 28 when they were not were 31.3% (18/58) and 0% (0/13), respectively.

Nordenram and Grave[21] studied bilateral mandibular third molar extractions in 39 FC− and 39 FC+ patients. One randomly selected molar in each pair was removed on the first day of the menstrual cycle and the other molar on the 14th day. Nordenram and Grave report an effect for both OC use and day of menstrual cycle. For FC− patients, AO rates for extractions on days 1 and 14 were 17.95% (7/39) and 7.69% (3/39), and for FC+ patients, the rates were 28.21% (11/39) and 17.95% (7/39). The higher rates during menstruation appear contradictory to the findings of Gersel-Pedersen.[19]

Brekke et al.[22] studied the effects of applying either a polylactic acid mesh or standard treatment to each of 228 pairs of mandibular third molars in a within-subject design. There were 89 males and 139 females, undefined in terms of OC use or menstrual cycle. Among males the AO rate (collapsed across conditions) was 6.38% (12/178), and in females the rate was 11.87% (33/278). The one-site-per-patient rates defined by treatments are shown in Table I.

Field et al.[23] observed the AO rate after 2787 extractions in assorted sites in 1322 males and 721 females. In males the rate was 3.40% (45 patients), and in females the rate was 5.55% (40 patients). Because these data are reported in terms of patients there is probably an underestimation of site-wise rates because multiple dry sockets in a single patient would be ignored.

Fridrich and Olson[24] studied 952 bilateral mandibular third-molar extractions in 476 patients with particular interest directed at the effects of several therapeutic modalities on AO rates. Although rates for sex and OC are published, the sample sizes for these groups are not. One is only informed that the effect of sex is not significant and that the effect of the FC− versus FC+ contrast is nearly significant (P = 0.0544). To use the data from this rather large study, the frequencies reported in Table I were arbitrarily estimated by assuming that half of subjects were male and half were female and that one fourth of females used OC. It should be noted that this backward esti-

mation process caused some distortion from reported AO rates.

Herpy and Goupil[25] recorded patient-wise AO rates in 150 males and 111 females after the removal of one or two mandibular third molars from each patient. In males the rate was 14.00% (21 patients), and in females the rate was 19.82% (22 patients).

Al-Khateeb et al.[7] studied the incidence of AO in Saudi Arabia. Six hundred forty-two third molars were removed from 283 males and 129 females, but the number of teeth that were removed was not reported by gender. Data were reconstructed from reported percentages under the assumption that the mean number of teeth was the same across gender lines. AO rates for M, FC−, and FC+ were 18.14% (80/441), 16.85% (31/184), and 23.53% (4/17), respectively.

Larsen[26] studied the effects of chlorhexidine or placebo rinse on AO rates in 278 bilaterally impacted mandibular third molars. Collapsing across the significant rinse factor, rates for M, FC−, and FC+ patients were 10.66% (13/122), 20.37% (22/108), and 10.42% (5/48), respectively. The relatively low AO rate for FC+ was attributed to contraceptive patients in this group tending to be younger and requiring less complicated extractions. Larsen[2] also reported site-wise AO rates after extraction of bilateral mandibular third molars. The rates in males, FC−, and FC+ were 14.00% (7/50), 25.00% (9/36), and 18.75% (3/16), respectively.

Chapnick and Diamond[27] also reported on AO rates as a function of gender, but these data are not presented here. It would appear that the surgical or evaluative methods in their study were quite different in that only five cases of AO were reported in 1021 extractions for an overall rate of 0.49%. These authors reported a higher rate for females (and females taking OC) since two of the five AO cases were in FC+ patients and a third case was in an FC− subject. However, there were more than twice as many females in their study as males and, therefore, rates were less for females although numbers were so low as to be statistically inconsequential.

THE META-ANALYSIS FRAMEWORK

Inferential limitations in narrative reviews of past research have lead to the development of meta-analysis methods. Meta-analysis involves (1) statistical methods that allow the merging of quantitative findings so that a combined estimate of effect (p-value and CI) can be calculated, and (2) the imposition of inclusion-exclusion (or other weighting) criteria so that selected studies are methodologically sound and address the research questions of interest.

Table II. Odds ratios for oral contraceptive-negative females compared with males

	Odds ratios		
Author	*All studies (exact 95% CI)*	*Mandibular third molars*	*One site per subject*
Krough[9]	1.096 (0.77-1.57)	Out	Out
Show[14]	1.416 (0.97-2.06)	In	In
Lilly et al.[15]	0.864 (0.57-1.29)	In	Out
Butler and Sweet[16] (175 ml lavage)	0.804 (0.16-3.52)	In	In
Butler and Sweet[16] (25 ml lavage)	0.582 (0.17-1.77)	In	In
Sweet and Butler[18]	6.527 (0.86-292)	In	Out
Gersel-Pederson[19]	4.579 (1.33-20.2)	In	Out
Fridich and Olson[24]	0.671 (0.43-1.03)	In	Out
Al-Khateeb et al.[7]	0.914 (0.56-1.47)	Out	Out
Larsen[26]	2.138 (097.-4.91)	In	Out
Larsen[2]	2.030 (0.59-7.25)	In	Out
P-value for homogeneity of ORs (B-D)	0.004	0.001	0.206
Mantel-Haenszel common OR	1.078	1.105	1.234
P-value (M-H, RBG variance)	0.349	0.309	0.207
95% confidence interval	0.921-1.262	0.912-1.340	0.890-1.712

Out = Data are omitted from analysis; in = data are included in analysis.

In many cases of meta-analysis the quantitative estimation of statistical effect is difficult because raw data are not available and one must combine and appropriately weight summary statistics. In the present study, this task is uncomplicated as contingency tables relating AO to the various binary risk indicators constitute "raw data" that can be combined with ordinary Mantel-Haenszel procedures.

The narrative review indicates that studies differed with respect to study populations, sites of extractions, and the potential influences of many confounding variables. In the face of such diversity, some have advocated the imposition of strict inclusion-exclusion criteria so that only studies of uniform design and of high methodologic quality are considered.[28]

However, it has been suggested that the effects of design and method are empirical rather than factual issues and should be evaluated within the context of the meta-analysis. If meta-analysis shows that studies evaluated as methodologically superior yield different results from the studies rated methodologically poorer, then final conclusions can be based on the "good" studies. If there is no difference in results, this finding disconfirms the methodological hypotheses. In such cases, all studies should be retained and included

Table III. Odds ratios for oral contraceptive positive females compared with males

Author	Odds ratios		
	All studies (exact 95% CI)	*Mandibular third molars*	*One site per subject*
Show[14]	4.425 (2.99-6.55)	In	In
Lilly et al.[15]	3.041 (2.00-4.55)	In	Out
Butler and Sweet[16] (175 ml lavage)	2.068 (0.19-13.0)	In	In
Butler and Sweet[16] (25 ml lavage)	2.978 (0.71-11.1)	In	In
Sweet and Butler[17, 18]	11.60 (1.27-557)	In	Out
Gersel-Pederson[19]	13.78 (2.57-80.5)	In	Out
Fridrich and Olson[24]	1.424 (0.83-2.39)	In	Out
Al-Khateeb et al.[7]	1.387 (0.32-4.65)	Out	Out
Larsen[26]	0.975 (0.26-314)	In	Out
Larsen[2]	1.410 (0.21-7.36)	In	Out
P-value for homogeneity of ORs (B-D)	0.001	0.001	0.588
Mantel-Haenszel common OR	2.778	2.853	4.164
P-value (M-H, RGB variance)	0.000	0.000	0.000
95% confidence interval	2.251-3.428	2.302-3.536	2.943-5.892

Out = Data are omitted from analysis; in = data are included in analysis.

Table IV. Odds ratios for assumed oral contraceptive mixed females compared with males

Author	Odds ratios		
	All studies (exact 95% CI)	*Mandibular third molars*	*One site per subject*
MacGregor[4]	1.575 (1.17-2.12)	Out	Out
Sweet and Butler[18] (175 ml lavage)	2.977 (0.33-143)	In	In
Sweet and Butler[18] (350 ml lavage)	5.539 (0.75-247)	In	In
Brekke et al.[22] (PLA−)	1.899 (0.83-4.66)	In	In
Brekke et al.[22] (PLA+)	1.957 (0.34-20.3)	In	In
Field et al.[23]	1.667 (1.05-2.64)	Out	Out
Herpy and Goupil[25]	1.516 (0.75-3.09)	In	Out
P-value of homogeneity of ORs (B-D)	0.730	0.518	0.474
Mantel-Haenszel common OR	1.682	1.971	2.455
P-value (M-H, RGB variance)	0.000	0.004	0.007
95% confidence interval	1.361-2.079	1.248-3.111	1.280-4.707

Out = Data are omitted from analysis; in = data are included in analysis.

in the final meta-analysis to provide the largest possible data base.[29]

Consistent with this latter perspective, the reviewed studies will be considered in their entirety and as subsets subject to design restrictions. These subsets are defined below, and differences in common OR estimates, across the subsets, serve to estimate the magnitude of methodologic effects.

STATISTICAL FINDINGS

Tables II, III, and IV present AO rates, ORs, and exact 95% CIs for FC−, FC+, and undefined females, respectively, compared with males for each study. In each table only those studies with relevant data are listed, and, based on the specific ORs considered in an analysis, three data sets are presented. The first set in each table includes all studies, the second set only studies on mandibular third molars, and the third set only considers studies on mandibular third molars when there are data for one site per subject. The second set is provided because findings for mandibular third molars are of particular clinical interest, and the third set is provided for statistical tractability. It should be noted that the number of studies remaining in the third subset is so small as to preclude the imposition of any further exclusion criteria. In those cases when there was a zero cell count, the reported study ORs were computed after one was added to each cell, but the original counts were used for computing common ORs.

For each set of studies the P-value for homogeneity of ORs (Breslow-Day), the Mantel-Haenszel (M-H) common OR statistic, a P-value for the M-H statistic (using Robins, Breslow, Greenland variance), and a 95% CI are computed. When more than one site has been studied per subject, P-values tend to be too small and CIs tend to be too narrow, improperly increasing likelihoods of nominal statistical significance. (However, the OR parameter estimate remains valid.) Therefore only the third set of each table of studies, which is limited to one site per subject data, provides P-values and CIs that can be considered valid.

Tables II, III, and IV show that FC negative females have an elevated risk for AO compared with

males, which is not statistically significant (OR = 1.23, CI = 0.89 to 1.71, one site per subject data). The increased risk for FC positive females, however, is significant (OR = 4.16, CI = 2.94 to 5.89). Females with unspecified OC status have an intermediate level of risk (OR = 2.46, CI = 1.28 to 4.71) presumably associated with some FC+. The findings across the complete data sets and the two subsets for each table are consistent with statistical conclusions being unchanged. Thus it would not appear that design or methodologic quality exerted dramatic effects. Although there is evidence that ORs are heterogeneous (and therefore the meaning of a common OR problematic) when either all or mandibular third molar studies are considered, ORs appear homogeneous for one-site-per-subject studies, which represent the data of principal interest. It should be noted that even when the common OR was statistically significant, the majority of individual study ORs was not, which suggests that many of these studies may have been underpowered to detect what might be considered meaningful gender effects.

Although contrasts between FC negative and positive females are not presented here, they are essentially identical to the male versus FC+ findings. They are also consistent with ORs that can be computed from the Nordenram and Grave[21] data. On cycle day 1, the OR for FC+ compared with FC− is 1.782, and on day 14 the OR is 2.594.

Only Catellani et al.[20] and Nordenram and Grave[21] present data on day-of-cycle effects; Catellani uses a between-subjects design, and Nordenram and Grave use a within-subjects design. Table V presents individual ORs for these three studies and a summary estimate. It is important to note that because cycle specifications are inconsistent and because studies consider both FC+ and FC− subjects, conclusions are difficult. Computation of ORs for the Nordenram and Grave data is also problematic. Although a within-subject design is used, the authors do not specify the group in which the "one case" of a patient developing AO in both operations occurred. For this reason this study was analyzed as a between-subjects design. When studies are considered together there was a statistically significant increase in AO risk associated with surgery early in the menstrual cycle (OR = 2.95, CI = 1.31 to 6.66), though none of the individual studies showed significant differences.

CLINICAL IMPLICATIONS

When information from many studies is considered together, there is strong statistical evidence that the use of OC (during some period in the menstrual cycle) is related to increased risk of AO. This suggests that hormonal factors should be considered in the scheduling of prophylactic or nonemergency exodontia. Based on the hypothesis that AO is caused in part by enhanced fibrinolytic activity associated with higher estrogen levels,[17] the present evidence suggests that FC+ females should be scheduled when they are in that part of the contraceptive cycle when they are not actually taking estrogen[20] or during a period of withdrawal.[21]

Table V. Odds ratios for time in cycle

Author	*Odds ratio (exact 95% CI)*
Catellani[5]	6.373 (0.85-289)
Nordenram and Grave[21] (FC−)	2.594 (0.54-16.8)
Nordenram and Grave[21] (FC+)	1.782 (0.54-6.22)
P-value for homogeneity of ORs (B-D)	0.247
Mantel-Haenszal common OR	2.949
P-value (M-H, RGB variance)	0.001
95% confidence interval	1.305-6.662

In the case of FC− females, there is insufficient published evidence on the effects of menstrual cycle. The only study on this issue[17] found a nonsignificant increase in AO rate on menstrual day 1 versus day 14 (first day of luteal phase). However, estrogen levels are not very different on these two days. Peak estrogen level occurs around day 11 at concentrations that can be 10 times that of day 1 and five times that of day 14. "Serum levels of estradiol rise from less than 50 pg/ml in the early follicular phase [day 6] to 200 to 500 pg/ml at midcycle and have a broad luteal-phase level of about 100 to 300 pg/ml."[30]

Hormonal effects on risk for AO associated with menstrual cycle in FC− females may be as great as those for FC+, but for a briefer period of time. This would account for increased (nonsignificant) risk in FC negative females compared with males, which would be slight because risk is averaged across the entire menstrual cycle. Although it might seem reasonable to avoid elective extractions during menstrual cycle days 10 to 12 (peak estrogen), this is inconsistent with Nordenram and Grave's[21] findings and recommendation to avoid the menstrual period on the basis of a reported increase in plasminogenic proactivators and activators in saliva during and near this time. The possibility that fibrinolytic activity has more than one peak within the menstrual cycle in women not taking OC clearly establishes the need for further empirical research.

Although the present analysis suggests an avoidable two- to threefold increase in AO because of OC and a possible effect because of menstrual cycle, studies in the past have not been optimally designed

or analyzed to remove the effects of various confounders. For example, because smoking rates have historically been higher in males and this increases AO risk,[2] this may have diminished the observed gender effect. Thus, actual increased risk in females may be greater than what has been estimated in this study.

The consistency of common OR estimates across the data subsets provides some evidence that design and methodology effects were not profound. However, for several of the research issues studied there is clearly insufficient data upon which to draw firm conclusions. We are presently involved in a large controlled study of AO rates in a military population designed to simultaneously consider gender-relevant risk factors and confounders, including day of OC/menstrual cycle, content and dosage of steroidal contraceptives including injectable and implantable, surgical difficulty, and smoking.

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19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Third Molar Extractions, Alveolar Osteitis, Sex, Oral Contraceptives

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Numerous literature references have suggested increased risk for localized alveolar osteitis associated with female gender, use of oral contraceptives, and point in menstrual/contraceptive cycle. However, the available information has not been systematically considered with the intent to accurately estimate the magnitude of these effects. The present review suggests that under certain conditions, some of which may be avoidable, females

may have at least a two to threefold increase in osteitis risk compared with males. It appears that this greater risk may be reduced by considering hormonal cycles when scheduling elective exodontia.